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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,590	12/14/2001	Jukka Salonen	0933-0179P	2024

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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 04/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/014,590	SALONEN, JUKKA	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-31* is/are pending in the application.

4a) Of the above claim(s) *1-12 and 24-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13, 15-23, and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☑ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 10/20/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed October 20, 2003 have been entered.

The addition of claims 29-31 is acknowledged.

Claims 1-13, and 15-31 are pending.

Claims 1-12 and 24-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

This application contains claims 1-12 and 24-28 drawn to an invention nonelected with traverse in Paper No. 7. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 13, 15-23, and 29-31 have been examined herein to the extent they read on the elected invention, insofar as they are not related to gene therapy.

The outstanding objection with regard to parenthesis use has been withdrawn in view of the amendments filed October 20, 2003.

The outstanding rejection under 35 USC 112, first paragraph with regard to the disorders reducing the protective effect of HDL has been withdrawn in view of the amendments filed October 20, 2003.

The outstanding rejection under 35 USC 112, first paragraph with regard to "protect" has been withdrawn in view of the amendments filed October 20, 2003.

The outstanding rejections under 35 USC 112, second paragraph have been withdrawn in view of the amendments filed October 20, 2003.

The outstanding rejections under 35 USC 102 have been withdrawn in view of the amendments filed October 20, 2003.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description requirement is established by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the invention. . .[emphasis added]." The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas,

etc., that fully set forth the claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). In the instant case, the specification fails to describe the genotyping mutations or polymorphisms that will influence serum or plasma γ-glutamyltransferase activity or concentration, or gnotyping for mutations in the phase I and II enzymes or the expression thereof. In the specification, page 5, line 17-29, it merely describes commonly known techniques to genotype DNA from blood sample. However, there is no description in the specification as to the specific mutation or polymorphism that will produce the activities or effects as recited in the claim. Examiner notes that such specific mutations and/or polymorphisms are important to the functions claimed (i.e., influencing the serum or plasma γ-glutamyltransferase activity or concentration, or genotyping for the mutations in the phase I and II enzymes or the expression thereof). Examiner further notes that the claim encompasses a wide array of molecules with different sequences. The specification does not disclose any of these variants, modifications or mutants, nor does it provide any teachings as to how the structures of these sequences relate to their function. Thus, the specification does not describe the complete structure of a representative number of species. Neither does the specification describe a representative number of species in terms of partial structure and relevant identifying characteristics. Absent of such teachings and guidance as to the structure-function relationship of these molecules, the specification does not describe the claimed molecules and the use thereof in such full, clear, concise and exact terms so as to indicate that Applicant had possession of these molecules and the use thereof at the

time of filing of the present application. Thus, the written description requirement has not been satisfied.

Response to arguments

Applicant's argument filed October 20, 2003 averring adequate written description being disclosed in the instant specification have been considered, but are not found persuasive. Applicant argues that the claims are not directed to the mutation and polymorphisms per se and therefore, the instant claims meet the requirements under 35 USC 112, first paragraph. Please note that even though the claims are nto drawn to the mutation and polymorphism per se, there is no description as to the mutation or polymorphisms that will influence serum or plasma γ-glutamyltransferase activity or concentration. In the instant specification, there is no specific mutation or polymorphism disclosed. Without the specification mutation or polymorphism disclosed, it is not clear how one can genotyping such mutation or polymorphisms as herein recited. Therefore, the claims are still considered properly rejected under 35 USC 112, first paragraph for lack of written description.

Response to Arguments

Applicant's arguments in regard to rejection under 35 USC 102 have been considered moot in view of the cancellation of the rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 13, 15, 17-23, and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Facts (Drug Facts and Comparisons, 1999, page 1082-1092, 1100), Lyons et al. (British Journal of Clinical Pharmacology, 1994;37:59-62) and Merck Manual (16th ed., page 408-412) in view of Boden (American Journal of Cardiology, 2000;86:12:19-22L), Navab et al., and Traub (Basic Skills in Interpreting Laboratory Data, chapter 9, page 121-129). All references of record in the previous office action.

Facts teaches gemfibrozil is useful to reduce coronary heart disease risk and also patients with hepatic dysfunction (liver damage) should not take gemfibrozil (See page 1100). Facts also teaches that HMG-CoA reductase inhibitor, pravastatin is known to reduce the risk of myocardial infarction (See page 1092). Facts also teaches that one of the contraindications of HMG-CoA reductase inhibitors is acute liver disease (i.e., liver damages) or unexplained persisent elevated liver function tests (See page 1084).

Lyons et al. teaches colestipol can enhance the HDL level (See abstract).

Merck Manual teaches that regular exercise can increase the HDL level (See page 412).

The references do not expressly teach the increase of HDL levels can reduce the risk of heart disease. The references do not expressly teach the testing liver damage and/or oxidative stress by checking checking the paraoxonase level, γ-glutamyl transferase (GGT) level and HDL oxidative capacity. The references do not expressly teach the exclusion of individual having liver damage and/or oxidative stress.

Boden teaches that HDL is one of the most significant risk factor for coronary artery disease with the increase of 1% of HDL resulting a 3% decrease of risk of heart disease (See the abstract; also page 21L-22L).

Navab et al. teaches the antioxidant effect of HDL is depending on paraoxonase and PAF acetylhydrolase (See page 835, col. 2 to page 837, col. 2; especially Fig.2 on page 836). Navab et al. also teaches that in certain conditions such as the acute phase response, the paraoxonase and PAF acetylhydrolase activities are reduced significantly even though the HDL level remains (See page 837, col. 1).

Traub teaches testing GGT level is known for checking the liver functions and damages (See page 127, col. 1-2). Traub also teaches that a marked elevated level of GGT might indicate alcoholic liver disease (See page 127, col. 1, last three paragraphs).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ gemfibrozil, pravastatin, colestipol, or exercise in

patients who is not having liver damage and/or oxidative stress to reduce the risk of heart disease.

One of ordinary skill in the art would have been motivated to employ gemfibrozil, pravastatin, colestipol, or exercise in patients who is not having liver damage and/or oxidative stress to reduce the risk of heart disease. It is known that gemfibrozil, pravastatin, exercise, and colestipol as useful to enhance the HDL levels, which can decrease the risk of heart disease. Therefore, treating patients that are free from liver damage, regardless of how the liver damage was diagnosed, for the reduction of risk in heart disease would be reasonably expected to be beneficial. Moreover, excluding the patients with low paraoxonase activity from the HDL enhancing treatment would be reasonable and obvious since the antioxidative protecting effect of HDL is depending on the level of paraoxonase. Therefore, it would be obvious to exclude patients who have low level of paraoxonase (note: oxidative stress) in order to make the drug-induced HDL increase effective for reducing the risk of cardiovascular disease.

Response to Arguments

Applicant's arguments filed October 20, 2003 averring Lyon's failure to teach the relationship between colestipol and liver function or oxidative stress have been fully considered but they are not persuasive. Lyon teaches colestipol can enhance HDL level and Boden teaches the increase of HDL can reduce the risk of developing heart disease. However, by merely increasing HDL level may not decreasing the risk of developing heart disease because as taught in Navab, patients under oxidative stress

such as patients having low level of paraoxonase activity may not be benefited from the increase of HDL. Therefore, possessing the teaching of the cited prior art, one of ordinary skill in the art would have been reasonably expected to employ colestipol to reduce the risk of heart diseases in patients that do not have oxidative stress or low level of paraoxonase activity.

Applicant's arguments filed October 20, 2003 in regard to the applicant's admission have been considered moot in view of the new ground of rejection.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Patent Examiner
Art Unit 1617